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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare Research and Quality

Scientific Information Request on Interventions to Improve Appropriate Antibiotic Use for Acute Respiratory Tract Infections

AGENCY: Agency for Healthcare Research and Quality (AHRQ), HHS.

ACTION: Request for Scientific Information Submissions

SUMMARY: The Agency for Healthcare Research and Quality (AHRQ) is seeking scientific information submissions from the public. Scientific information is being solicited to inform our review of Interventions to Improve Appropriate Antibiotic Use for Acute Respiratory Tract Infections, which is currently being conducted by the Evidence-based Practice Centers for the AHRQ Effective Health Care Program. Access to published and unpublished pertinent scientific information will improve the quality of this review. AHRQ is conducting this systematic review pursuant to Section 1013 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Public Law 108-173, and Section 902(a) of the Public Health Service Act, 42 U.S.C. 299a(a).

DATES: Submission Deadline on or before [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES:

Online submissions: <http://effectivehealthcare.AHRQ.gov/index.cfm/submit-scientific-information-packets/>. Please select the study for which you are submitting information from the list to upload your documents.
E-mail submissions: SIPS@epc-src.org.

Print submissions

Mailing Address:

Portland VA Research Foundation

Scientific Resource Center

ATTN: Scientific Information Packet Coordinator

PO Box 69539 Portland, OR 97239

Shipping Address (FedEx, UPS, etc.):

Portland VA Research Foundation

Scientific Resource Center

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3710 SW U.S. Veterans Hospital Road

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FOR FURTHER INFORMATION CONTACT:

Ryan McKenna, Telephone: 503-220-8262 ext. 58653 or Email: SIPS@epc-src.org.

SUPPLEMENTARY INFORMATION:

The Agency for Healthcare Research and Quality has commissioned the Effective Health Care (EHC) Program Evidence-based Practice Centers to complete a review of the evidence for Interventions to Improve Appropriate Antibiotic Use for Acute Respiratory Tract Infections.

The EHC Program is dedicated to identifying as many studies as possible that are relevant to the questions for each of its reviews. In order to do so, we are supplementing the usual manual and electronic database searches of the literature by requesting information from the public (e.g., details of studies conducted). We are looking for studies that report on Interventions to Improve Appropriate Antibiotic Use for Acute Respiratory Tract Infections, including those that describe adverse events. The entire research protocol, including the key questions, is also available online at: <http://effectivehealthcare.AHRQ.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=1913>

This notice is to notify the public that the EHC Program would find the following information on Interventions to Improve Appropriate Antibiotic Use for Acute Respiratory Tract Infections helpful:

- A list of completed studies that your company has sponsored for this indication. In the list, indicate whether results are available on ClinicalTrials.gov along with the ClinicalTrials.gov trial number.
- For completed studies that do not have results on ClinicalTrials.gov, please provide a summary, including the following elements: study number, study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, primary and secondary outcomes, baseline characteristics, number of patients screened/eligible/enrolled/lost to follow-up/withdrawn/analyzed, effectiveness/efficacy, and safety results.
- A list of ongoing studies your company has sponsored for this indication. In the list, please provide the ClinicalTrials.gov trial number or, if the trial is not registered, the protocol for the study including a study number, the study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, and primary and secondary outcomes.
- Description of whether the above studies constitute ALL Phase II and above clinical trials sponsored by your company for this indication and an index outlining the relevant information in each submitted file.

Your contribution is very beneficial to the EHC Program. Since the contents of all submissions will be made available to the public upon request, materials submitted must be publicly available or can be made public. Materials that are considered confidential; marketing materials; study types not included in the review; or information on indications not included in the review cannot be used by the EHC Program. This is a voluntary request for information, and all costs for complying with this request must be borne by the submitter.

The draft of this review will be posted on AHRQ's EHC Program website and available for public comment for a period of 4 weeks. If you would like to be notified when the draft is posted, please sign up for the e-mail list at: <http://effectivehealthcare.AHRQ.gov/index.cfm/join-the-email-list1/>.

The systematic review will answer the following questions. This information is provided as background. AHRQ is not requesting that the public provide answers to these questions. The entire research protocol, is also available online at: <http://effectivehealthcare.AHRQ.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=1913>

The Key Questions

Key Question 1

For patients with an acute respiratory tract infection (RTI) and no clear indication for antibiotic treatment, what is the comparative effectiveness of particular strategies in improving the appropriate prescription or use of antibiotics compared with other strategies or standard care?

- I. Does the comparative effectiveness of strategies differ according to how appropriateness is defined?
- II. Does the comparative effectiveness of strategies differ according to the intended target of the strategy (i.e., clinicians, patients, and both)?
- III. Does the comparative effectiveness of strategies differ according to patient characteristics, such as type of Rh, signs and symptoms (nature and duration), when counting began for duration of symptoms, previous medical history (e.g., frailty, comorbidity), prior RTIs, and prior use of antibiotics, age, ethnicity, socioeconomic status, and educational level attained?
- IV. Does the comparative effectiveness of strategies differ according to clinician characteristics, such as specialty, number of years in practice, type of clinic organization, geographic region, and population served?
- V. Does the comparative effectiveness differ according to the diagnostic method or definition used, the clinician's perception of the patient's illness severity, or the clinician's diagnostic certainty?
- VI. Does the comparative effectiveness differ according to various background contextual factors, such as the time of year, known patterns of disease activity (e.g., an influenza epidemic, a pertussis outbreak), system-level characteristics, or whether the intervention was locally tailored?

Key Question 2

For patients with an acute RTI and no clear indication for antibiotic treatment, what is the comparative effect of particular strategies on antibiotic resistance and medical complications (including mortality and adverse effects of receiving or not receiving antibiotics) compared with other strategies or standard care?

- I. Does the comparative effect of strategies differ according to the intended target of the strategy (i.e., clinicians, patients, and both)?
- II. Does the comparative effect of strategies differ according to patient characteristics, such as type of RTI, signs and symptoms (nature and duration), when counting began for duration of

symptoms, previous medical history (e.g., frailty, comorbidity), prior RTIs, prior use of antibiotics, age, ethnicity, socioeconomic status, and educational level attained?

- III. Does the comparative effect of strategies differ according to clinician characteristics, such as specialty, number of years in practice, type of clinic organization, geographic region, and population served?
- IV. Does the comparative effectiveness differ according to the diagnostic method or definition used, the clinician's perception of the patient's illness severity, or the clinician's diagnostic certainty?
- V. Does the comparative effect differ according to various background contextual factors, such as the time of year, known patterns of disease activity (e.g., an influenza epidemic, a pertussis outbreak), whether the intervention was locally tailored, system-level characteristics, or the source of the resistance data (i.e., population versus study sample)?

Key Question 3

For patients with an acute RTI and no clear indication for antibiotic treatment, what is the comparative effect of particular strategies on other clinical outcomes (e.g., hospitalization, health care utilization, patient satisfaction) compared with other strategies or standard care?

- I. Does the comparative effect of strategies differ according to the intended target of the strategy (i.e., clinicians, patients, and both)?
- II. Does the comparative effect of strategies differ according to patient characteristics, such as type of RTI, signs and symptoms (nature and duration), when counting began for duration of symptoms, previous medical history (e.g., frailty, comorbidity), prior RTIs, prior use of antibiotics, age, ethnicity, socioeconomic status, and educational level attained?
- III. Does the comparative effect of strategies differ according to clinician characteristics, such as specialty, number of years in practice, type of clinic organization, geographic region, and population served?
- IV. Does the comparative effectiveness differ according to the diagnostic method or definition used, the clinician's perception of the patient's illness severity, or the clinician's diagnostic certainty?
- V. Does the comparative effect differ according to various background contextual factors, such as the time of year, known patterns of disease activity (e.g., an influenza epidemic, a pertussis

outbreak), whether the intervention was locally tailored or system-level characteristics?

Key Question 4

For patients with an acute RTI and no clear indication for antibiotic treatment, what is the comparative effect of particular strategies on achieving intended intermediate outcomes, such as improved knowledge regarding use of antibiotics for acute RTIs (clinicians and/or patients), improved shared decision making regarding the use of antibiotics, and improved clinician skills for appropriate antibiotic use (e.g., communication appropriate for patients' literacy level and/or cultural background)?

Key Question 5

What are the comparative non-clinical adverse effects of strategies for improving the appropriate use of antibiotics for acute RTIs (e.g., increased time burden on clinicians, patients, clinic staff)?

The following inclusion/exclusion criteria reflect input from key informants, public comments, AHRQ and the TEP.

PICOTS (POPULATION, INTERVENTIONS, COMPARATORS, OUTCOMES, TIMING, SETTING)

Populations

- I. Adult and pediatric patients with an acute RTI and no clear indication for antibiotic treatment. Respiratory tract infections of interest include: acute bronchitis; otitis media; sore throat/pharyngitis/tonsillitis; rhinitis; sinusitis; cough and common cold.
- II. Parents of pediatric patients with acute RTI and no clear indication for antibiotic treatment.
- III. Healthy adults and/or children without a current acute RTI, who may develop an acute RTI in the future.
- IV. Clinicians and others who care for patients with acute RTI in outpatient settings.
- V. Groups whose attendance policies may indirectly affect the use of antibiotics, such as employers or school officials.

Interventions

Any strategy for improving appropriate use of antibiotics when not indicated for acute RTI, which may fall into various categories, including:

- I. Educational, behavioral and psychological interventions that target clinicians, patients, or both.
- II. Strategies to improve communication between clinicians and patients, such as those designed to improve shared decision making.
- III. Clinical strategies, such as delayed prescribing of antibiotics, clinical prediction rules, use of risk assessment or diagnostic prediction, use of non-antibiotic alternatives, or use of relevant point-of-care (POC) diagnostic tests.
 - A. EPC will include any POC test that is available and used in primary care settings for diagnostic purposes with the ability to provide results within a reasonable period (e.g. during the clinic visit). Examples include inflammatory tests (e.g., procalcitonin, c-reactive protein [CRP], white blood cell, etc.), rapid multiplex polymerase chain reaction (PCR) tests used to rule in/out organisms (e.g. rapid strep test, influenza, RSV), routine diagnostic tests, such as chest x-ray, pulse oximetry, and blood gasses, when they are specifically evaluated as an intervention for improving antibiotic use.
- IV. System level strategies, such as clinician reminders (paper-based or electronic), clinician audit and feedback, financial or regulatory incentives for clinicians or patients, antimicrobial stewardship programs, pharmacist review.
- V. Multifaceted approaches that include numerous elements of one or more of the above strategies.

Comparators

- I. Different strategies for improving appropriate use of antibiotics when not indicated for acute RTI.
- II. Standard care without a strategy for improving appropriate use of antibiotics.

Outcomes

Key Question 1

- Increased appropriate prescription of antibiotics (primary outcome)

- Increased appropriate use of antibiotics (primary outcome)

Note: Studies may vary in how appropriateness is defined or determined. We will accept and record any definition of appropriateness. We will group together studies that use similar definitions of appropriateness and categorize the different groups based on concordance with (e.g., high, medium, low) select clinical practice guidelines (e.g., AAP, ACCP, AAFP). We will then evaluate whether the comparative effectiveness of strategies differ across categories. We may also find that overall reduction in antibiotic prescription or use is reported, without a determination of appropriateness. While this is not a direct measure of the primary outcomes, we will report these as indirect measures of the impact of the intervention.

Key Question 2

- Mortality
- Antibiotic resistance
- Medical complications
- Adverse drug effects, including clostridium difficile infections

Key Question 3

- Admission to hospital
- Clinic visits (Index, return and subsequent episodes), ED visits
- Time to return to work and/or school
- Patient satisfaction
- Quality of life
- Improvement in patient symptoms, speed of improvement
- Use of non-antibiotic treatments, such as over-the-counter medications
- Utilization of vaccinations
- Quality metrics

Key Question 4

Intermediate outcomes, such as improved knowledge regarding use of antibiotics for acute RTI (clinician and/or patient), or improved shared decision making

Key Question 5

Adverse effects of the strategy, such as increased time burden on clinicians, sustainability of intervention (e.g. measures of continued effectiveness over time), diagnostic resource use associated with POC testing, diagnostic coding (e.g. ICD billing codes) according to desired action (prescribe/not prescribe)

Timing

Any duration of follow-up.

Setting

- I. Outpatient care settings including institutional settings
- II. Emergency care settings
- III. Other settings, such as school or workplace

Study design

We will prioritize comparative studies with concurrent control groups (e.g. randomized controlled trial, prospective and retrospective cohort studies including database studies). For areas in which direct comparative evidence is lacking, we will include before-after studies, with or without a control group and with or without repeated measures.

Dated: June 16 2014.

Richard Kronick,
AHRQ Director.